Amendments to the Specification:

Please replace paragraph [0001] with the following amended paragraph:

[0001] This application is a continuation of U.S. Application No. 10/328,495, filed December 23, 2002, now U.S. Patent No. 6,693,130, which is a continuation of U.S. Application No. 09/721,261, now U.S. Patent No. 6,531,506, which is a ~~continuation in part~~ continuation-in-part of U.S. Application ~~No~~ No. 09/252,148, filed February 18, 1999, now U.S. Patent No. 6,150,415. The disclosures of all of these applications are incorporated herein by reference.

Please replace paragraph [0034] with the following amended paragraph:

[0034] As noted above, a preferred class of inhibitors of the invention are compounds shown by Formulas 1 and 2, above. Means for preparing such compounds and assaying desired compounds for the ability to inhibit epoxide hydrolases is described in the parent application, ~~USSN~~ U.S. Application No. 09/252,148, now U.S. Patent No. 6,150,415. Compounds of Formula 2 are described in U.S. Patent No. 5,955,496 and in International Patent Application Publication No. WO98/06261.

Please replace replacement paragraph [0065] as found in the Preliminary Amendment filed June 14, 2005 with the following rewritten paragraph:

[0065] EET hydrolysis. Racemic ~~[1-14C]EETs~~ [1-^{14}C]EETs were synthesized and purified according to published methods from ~~[1-14C]~~ [1-^{14}C]arachidonic acid (56-57 μCi/μmole) by nonselective epoxidation (Falck, J.R. et al., Meth Enzymol 187, 357-364 (1990)). Hydrolysis of ~~[1-14C]~~ [1-^{14}C]EETs was measured in WKY and SHR renal S9 fractions at 37°C as described previously (Zeldin, D.C. et al. J Biol Chem 268, 6402-6407 (1993)). The reaction mixture consisted of 50 μM EET (0.045-0.09 μCi) and 1 mg/ml S9 protein (0.5 mg/ml SHR S9 protein for 14,15-EET hydrolysis) in 150 mM KCl, 10 mM ~~MgCl2~~ $MgCl_2$, 50 mM potassium phosphate

buffer pH 7.4. Reactions were carried out for 40 min (10 min for 14,15-EET hydrolysis in SHR samples) and the reaction products were extracted into ethyl acetate, evaporated under a blanket of nitrogen and detected by reverse phase HPLC with radiometric detection as described for arachidonic acid incubations.

Please replace paragraph [0066] with the following amended paragraph:

[0066] DHET urinary excretion. Urinary creatinine concentrations were measured by the Medical Center Clinical Laboratories at the University of California San Francisco. Methods used to quantify endogenous EETs and DHETs present in rat urine were similar to those described by Capdevila et al. (Capdevila, J.H. et al. J Biol Chem 267, 21720-21726 (1992)). DHET and ~~[1-14C]~~ [1-^{14}C]DHET internal standards were prepared by chemical hydration of EETs and ~~[1-14C]~~ [1-^{14}C]EETs as described (Zeldin, D.C. et al. J Biol Chem 268, 6402-6407 (1993)). All synthetic EETs and DHETs were purified by reverse-phase HPLC. EET quantification were made by GC/MS analysis of their pentafluorobenzyl (PFB) esters with selected ion monitoring at m/z 319 (loss of PFB from endogenous EET-PFB) and m/z 321 (loss of PFB from ~~[1-14C]~~ [1-^{14}C]EET-PFB internal standard). The EET-PFB/~~[1-14C]~~ [1-^{14}C]EET-PFB ratios were calculated from the integrated values of the corresponding ion current intensties. Quantifications of DHETs were made from GC/MS analysis of their PFB esters, trimethylsilyl (TMS) ether with selected ion monitoring at m/z 481 (loss of PFB from endogenous DHET-PFB-TMS) and m/z 483 (loss of PFB from ~~[1-14C]~~ [1-^{14}C]DHET-PFB-TMS internal standard). The DHET-PFB-TMS/~~[1-14C]~~ [1-^{14}C]DHET-PFB-TMS ratios were calculated from the integrated values of the corresponding ion current intensities. Data were normalized for kidney function by expressing per mg creatinine. Control studies demonstrated that under the conditions used, artifactual EET or DHET formation was negligible.

Please replace replacement paragraph [0074] as found in the Preliminary Amendment filed June 14, 2005, with the following rewritten paragraph:

[0074] A tight binding sEH specific inhibitor, dicylcohexylurea (DCU) (Morisseau, C. et al., Proc Natl Acad Sci USA 96, 8849-8854 (1999)), was used to reduce sEH activity in vivo and to determine the effect of decreased EET hydrolysis on blood pressure. Inhibition of EET hydrolysis by DCU was confirmed in incubations of renal S9 fractions with the regioisomeric EETs (Figure 4A). A dose-dependent inhibition of EET hydrolysis by DCU was apparent for all three regioisomers. DCU had the most significant effect on the hydrolysis of 8,9-EET, inhibiting the reaction with an IC50 of 0.086 ± 0.014 μM. The corresponding IC50 values for inhibition of 11,12- and 14,15-EET hydrolysis were 0.54 ± 0.08 μM and 0.45 ± 0.16 μM respectively. At concentrations up to 25 μM, DCU had no effect on CYP epoxygenase or ω-hydroxylase activity and previous studies from our laboratory have shown that DCU does not inhibit mEH (Morisseau, C. et al., Proc Natl Acad Sci USA 96, 8849-8854 (1999). The potent inhibition of sEH by DCU was confirmed with purified rat sEH. DCU inhibited sEH-catalyzed tDPPO hydrolysis with a Ki of 34 nM. This is comparable to the Ki values for DCU with human (30 nM) and murine (26 nM) sEH , (Morisseau, C. et al., Proc Natl Acad Sci USA 96, 8849-8854 (1999).

Please replace replacement paragraph [0076] as found in the Preliminary Amendment filed June 14, 2005 with the following rewritten paragraph:

[0076] A study of the time course of the effect of a single dose of DCU (3 mg/kg) demonstrated that the antihypertensive effect in the SHR was acute (Figure 4C). Blood pressure was decreased 22 ± 4 mm Hg 6 hr after DCU treatment ($p < 0.01$) and returned to baseline levels by 24 hr after the dose. Importantly, there was no effect of DCU on blood pressure in the WKY (Figure 4D). This is consistent with the very low levels of sEH protein in the WKY kidney. Several additional structurally related inhibitors were also studied in the SHR. N-cyclohexyl-N'-dodecylurea is a sEH inhibitor with similar potency to DCU (IC50 with mouse sEH = 0.05 ± 0.01 μM compared to 0.09 ± 0.01 μM ~~M~~ for DCU; see Table 1 above ~~unpublished data, C. Morisseau and B. Hammock, 2000~~). A single dose of N-cyclohexyl-N'-dodecylurea significantly decreased systolic blood pressure 12 ± 2 mm Hg 6 hr after the dose, and similar to

DCU, blood pressure returned to normal by 24 hours after the dose (Figure 5). The N-cyclohexyl-N'-ethylurea analog is a weak sEH inhibitor (IC50 with mouse sEH = 51.7 μM, ~~M;~~ ~~unpublished data, C. Morisseau and B. Hammock, 2000~~ see Table 1 above) and had no effect on blood pressure in the SHR. Likewise, the selective mEH inhibitor dodecylamine also had no effect on blood pressure. Collectively, these data suggest that the effect of DCU and N-cyclohexyl-N'-dodecylurea on blood pressure is related to their ability to inhibit sEH and EET hydrolysis in vivo.